ONE MINUTE CONSULT

BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Should the actual or the corrected serum sodium be used to calculate the anion gap in diabetic ketoacidosis?

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A: ONE SHOULD USE the actual, measured sodium concentration to calculate the anion gap,[1] and use the corrected sodium concentration to estimate the severity of dehydration in severe hyperglycemia.

Use the anion gap to evaluate ketoacidosis

The anion gap (the serum sodium concentration minus the sum of the serum chloride and bicarbonate concentrations) is useful in estimating the concentration of other anions not usually measured—notably, ketones such as beta-hydroxybutyrate and acetoacetate.

Why use the measured sodium and not the corrected sodium? The anion gap reflects the balance between positively and negatively charged constituents of extracellular fluid. Although we adjust the sodium value according to the glucose value to evaluate dehydration, glucose is electrically neutral and does not affect the anion gap. (It does, however, contribute to body fluid osmolality and influences water shifts between the intracellular and the extracellular fluid.) The corrected sodium value would distort the anion gap.

Hyponatremia or hypernatremia (due to water gain or loss) affects the anion gap, but only slightly. TABLE 1 demonstrates the theoretic effect on the normal anion gap in the case of a 10% gain or 10% loss of water. Since all of the components of the anion gap calculation are concentrated or diluted to the same extent, the anion gap is minimally altered—too little to interfere with proper interpretation of the acid-base status.

Use corrected sodium to evaluate dehydration

On the other hand, correcting the serum sodium concentration in patients with severe hyperglycemia is very useful in estimating the magnitude of water loss that has occurred during the development of hyperglycemia. The most commonly used formula for correction is to add 1.6 mmol/L to the measured serum sodium concentration for every 100-mg/dL increase in glucose, although other conversion factors have been suggested.[2]

If the corrected sodium concentration is elevated, the patient is markedly dehydrated and needs hypotonic fluids as an important part of management. If the corrected sodium concentration is normal despite a very high serum glucose concentration, either the patient has maintained adequate water intake or the onset of hyperglycemia was very acute. In the latter case, the decreased serum sodium concentration will very likely return to normal merely by giving insulin to correct the hyperglycemia.

Using the corrected sodium distorts the anion gap

TABLE 1

Theoretic effect of water gain or loss on the normal anion gap

	SODIUM	CHLORIDE	BICARBONATE	ANION GAP
Normal hydration	140 mmol/L	105.0 mmol/L	25.0 mmol/L	10 mmol/L
10% gain of water	126 mmol/L	94.5 mmol/L	22.5 mmol/L	9 mmol/L
10% loss of water	154 mmol/L	115.5 mmol/L	27.5 mmol/L	11 mmol/L

HOW COMMON IS 'NON-GAP' ACIDOSIS?

Diabetic ketoacidosis is often not a "pure" high anion-gap acidosis at presentation, and it almost invariably goes through a "non-gap" phase during recovery.

Metabolic acidosis may be of two types[1]: acidosis with an increased anion gap (usually due to organic acids), and acidosis with a normal anion gap, usually due to hyperchloremia and called hyperchloremic acidosis.

In a case series in Greece,[3] of 40 patients with diabetic ketoacidosis, 53% had ketoacidosis with an increased anion gap, and 18% had acidosis with an increased anion gap combined with hyperchloremic acidosis. Hyperchloremic acidosis was also common in a larger US case series.[4]

In both series, hydration status was directly related to the degree of retention of unmeasured anions: ie, patients with the highest degree of volume depletion were most likely to have a large anion gap.

Oh et al[5] noted a somewhat different pattern, however. In 35 patients with diabetic ketoacidosis, the increase in anion gap exactly paralleled the fall in bicarbonate. However, during recovery, these patients all developed a hyperchloremic type of metabolic acidosis.

DKA can go through a 'non-gap' phase during recovery

Understanding 'non-gap' acidosis

The mechanism of hyperchloremic acidosis in diabetic ketoacidosis is best understood by considering the consequences of adding a large quantity of beta-hydroxybutyric acid to the extracellular fluid, as occurs early in the development of diabetic ketoacidosis. Initially, each hydrogen ion combines with a bicarbonate, "destroying" it to produce CO_2 and water. The accompanying anion (in this case beta-hydroxybutyrate) is retained in the plasma and is an "unmeasured" anion. However, because the clearance of ketoacid anions by the kidney is relatively high, as long as volume depletion is avoided and the glomerular filtration rate is adequate, many of these unmeasured anions will be excreted in the urine along with accompanying cations (sodium or potassium).

This wasting of ketone salts produces a contraction of extracellular fluid volume and signals the kidney to retain dietary or infused sodium chloride. As a result, the bicarbonate in the extracellular fluid remains at a reduced level while the anion gap is diminished, due to a relative hyperchloremia.

In some patients in whom ketoacidosis develops more slowly, there may be large losses of these anions in the urine, with increasing acidosis (reflected by the low bicarbonate) that is not reflected by an accompanying increase in the anion gap.

Ketoacid anions as potential bicarbonate

Another way of understanding the development of acidosis with a normal anion gap is by recognizing that the ketoacid anions beta-hydroxybutyrate and acetoacetate are potential bicarbonate ions. If they are retained in the body, they metabolize back to bicarbonate when adequate insulin is provided. Therefore, the loss of sodium hydroxybutyrate and sodium acetoacetate in the urine has exactly the same consequence as the loss of sodium bicarbonate in the urine: hyperchloremic metabolic acidosis.

As Oh et al noted,[5] this occurs in almost all patients as they are treated for diabetic ketoacidosis—even patients presenting with an increased anion gap develop transient hyperchloremic acidosis during recovery.

Because acidosis with a normal anion gap is principally due to the renal loss of ketone salts (specifically, bicarbonate precursors), recovery is usually slower. The acidosis will persist unless the patient is given exogenous sodium bicarbonate or until the kidney has had time to generate new bicarbonate through the secretion of hydrogen ions.

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